# EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 2 | ("6949584").PN. | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:01 |
| L2 | 438 | (514/475).CCLS. | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:02 |
| L3 | 6 | TNP-470 adj conjugate | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:10 |
| L4 | 11 | Ronit.inv. and Satchi.inv. | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:12 |
| L5 | 120 | Judah.inv. and Folkman.inv. | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:11 |
| L6 | 11 | Ronit.inv. and Satchi.inv. | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:12 |

# EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 2 | ("6949584").PN. | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:01 |
| L2 | 438 | (514/475).CCLS. | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:02 |
| L3 | 6 | TNP-470 adj conjugate | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:10 |
| L4 | 11 | Ronit.inv. and Satchi.inv. | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:12 |
| L5 | 120 | Judah.inv. and Folkman.inv. | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:11 |
| L6 | 11 | Ronit.inv. and Satchi.inv. | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | OFF | 2006/10/02 16:12 |

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1611bxv

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

| | | |
|---|---|---|
| NEWS 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS 2 | | "Ask CAS" for self-help around the clock |
| NEWS 3 | FEB 27 | New STN AnaVist pricing effective March 1, 2006 |
| NEWS 4 | MAY 10 | CA/CAplus enhanced with 1900-1906 U.S. patent records |
| NEWS 5 | MAY 11 | KOREAPAT updates resume |
| NEWS 6 | MAY 19 | Derwent World Patents Index to be reloaded and enhanced |
| NEWS 7 | MAY 30 | IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2 |
| NEWS 8 | MAY 30 | The F-Term thesaurus is now available in CA/CAplus |
| NEWS 9 | JUN 02 | The first reclassification of IPC codes now complete in INPADOC |
| NEWS 10 | JUN 26 | TULSA/TULSA2 reloaded and enhanced with new search and and display fields |
| NEWS 11 | JUN 28 | Price changes in full-text patent databases EPFULL and PCTFULL |
| NEWS 12 | JUl 11 | CHEMSAFE reloaded and enhanced |
| NEWS 13 | JUl 14 | FSTA enhanced with Japanese patents |
| NEWS 14 | JUl 19 | Coverage of Research Disclosure reinstated in DWPI |
| NEWS 15 | AUG 09 | INSPEC enhanced with 1898-1968 archive |
| NEWS 16 | AUG 28 | ADISCTI Reloaded and Enhanced |
| NEWS 17 | AUG 30 | CA(SM)/CAplus(SM) Austrian patent law changes |
| NEWS 18 | SEP 11 | CA/CAplus enhanced with more pre-1907 records |
| NEWS 19 | SEP 21 | CA/CAplus fields enhanced with simultaneous left and right truncation |
| NEWS 20 | SEP 25 | CA(SM)/CAplus(SM) display of CA Lexicon enhanced |
| NEWS 21 | SEP 25 | CAS REGISTRY(SM) no longer includes Concord 3D coordinates |
| NEWS 22 | SEP 25 | CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine |
| NEWS 23 | SEP 28 | CEABA-VTB classification code fields reloaded with new classification scheme |
| NEWS 24 | OCT 02 | MARPAT(R) now updated daily |

| | |
|---|---|
| NEWS EXPRESS | JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006. |
| NEWS HOURS | STN Operating Hours Plus Help Desk Availability |
| NEWS LOGIN | Welcome Banner and News Items |
| NEWS IPC8 | For general information regarding STN implementation of IPC 8 |
| NEWS X25 | X.25 communication option no longer available |

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation

of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:55:23 ON 02 OCT 2006

=> FILE CAPLUS

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'CAPLUS' ENTERED AT 14:55:42 ON 02 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE COVERS 1907 - 2 Oct 2006 VOL 145 ISS 15
FILE LAST UPDATED: 1 Oct 2006 (20061001/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

```
=> s TNP-470
          2450 TNP
         23366 470
L1         487 TNP-470
               (TNP(W)470)

=> s l1 and plymer
             1 PLYMER
L2           0 L1 AND PLYMER

=> s l1 and polymer
       1088156 POLYMER
L3           8 L1 AND POLYMER

=> s l1 and conjugate
         66197 CONJUGATE
L4          14 L1 AND CONJUGATE

=> s l4 or l3
L5          17 L4 OR L3

=> d l5 1-17 bib ABS

L5   ANSWER 1 OF 17  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2006:796478  CAPLUS
```

DN 145:180960
TI Method for monitoring early treatment response
IN Norfray, Joseph F.
PA Receptomon, LLC, USA
SO U.S. Pat. Appl. Publ., 12pp., Cont.-in-part of U.S. Ser. No. 53,059.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2006177378 | A1 | 20060810 | US 2005-193037 | 20050729 |
| | US 2006177377 | A1 | 20060810 | US 2005-53059 | 20050208 |
| | WO 2006086159 | A2 | 20060817 | WO 2006-US2675 | 20060126 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

| | | | |
|---|---|---|---|
| PRAI | US 2005-53059 | A2 | 20050208 |
| | US 2005-193037 | A | 20050729 |

AB Disclosed is a method for monitoring early treatment response of a cancer treatment comprising measuring by magnetic resonance spectroscopy (MRS), for example, proton MRS, the amount of Choline present in the tissue adjoining or surrounding the cancerous tissue before and after treatment; the treatment comprises administration of an angiogenesis inhibitor, for example, a VEGF inhibitor, whereby a decrease in the amount of Choline after treatment is indicative of a pos. response. The decrease in the amount of Choline represents the decrease in the internal cell membrane as a result of down regulation of the organelles and their secretory granules and their transport vesicles. Disclosed also is a method for determining effectiveness of an angiogenesis inhibitor in the treatment of cancer. Also disclosed are methods of monitoring early treatment response in diseases where an angiogenesis effector, i.e., an inhibitor or promoter of angiogenesis, is employed. Also disclosed is a method for monitoring protein translation related to angiogenesis.

L5 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:796477 CAPLUS
DN 145:180959
TI Method for monitoring early treatment response
IN Norfray, Joseph F.
PA Receptomon, Llc., USA
SO U.S. Pat. Appl. Publ., 11pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2006177377 | A1 | 20060810 | US 2005-53059 | 20050208 |
| | US 2006177378 | A1 | 20060810 | US 2005-193037 | 20050729 |
| | WO 2006086159 | A2 | 20060817 | WO 2006-US2675 | 20060126 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRAI US 2005-53059 A2 20050208
US 2005-193037 A 20050729

AB Disclosed is a method for monitoring early treatment response of a cancer treatment comprising measuring by magnetic resonance spectroscopy (MRS), for example, proton MRS, the amount of Choline present in the tissue adjoining or surrounding the cancerous tissue before and after treatment; the treatment comprises administration of an angiogenesis inhibitor, for example, a VEGF inhibitor, whereby a decrease in the amount of Choline after treatment is indicative of a pos. response. The decrease in the amount of Choline represents the decrease in the internal cell membrane as a result of down regulation of the organelles and their secretory granules and their transport vesicles. Disclosed also is a method for determining effectiveness of an angiogenesis inhibitor in the treatment of cancer. Also disclosed are methods of monitoring early treatment response in diseases where an angiogenesis effector, i.e., an inhibitor or promoter of angiogenesis, is employed.

L5 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:790844 CAPLUS
DN 145:202923
TI Method using an anti-VEGF monoclonal antibody and a HPMA copolymer-TNP-470 conjugate for treatment of angiogenic diseases
IN Folkman, Judah; Satchi-Fainaro, Ronit
PA Children's Medical Center Corporation, USA
SO PCT Int. Appl., 45pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2006084054 | A2 | 20060810 | WO 2006-US3712 | 20060202 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-649235P P 20050202

AB The invention discloses methods for treating cancer and angiogenic diseases comprising administering an anti-VEGF (vascular endothelial growth factor) monoclonal antibody (e.g. Avastin) and a N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer-TNP-

470 conjugate (e.g. Caplostatin) to a patient in need thereof. Preparation of HPMA copolymer-TNP-470 conjugate is described.

L5 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:736387 CAPLUS
DN 145:180945
TI Lipocalin 2 in reversing epithelial to mesenchymal transition and for treatment or prevention of cancer metastasis, angiogenesis, and fibrosis
IN Sukhatme, Vikas P.; Karumanchi, S. Ananth; Seth, Pankaj; Hanai, Junichi; Mammoto, Tadanori; Barasch, Jonathan; Mori, Kiyoshi
PA Beth Israel Deaconess Medical Center, USA
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2006078717 | A2 | 20060727 | WO 2006-US1738 | 20060119 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-645438P P 20050119
AB The invention invention shows lipocalin 2 in reversing epithelial to mesenchymal transition and for treatment or prevention of cancer metastasis, angiogenesis, and fibrosis. Lipocalin 2 suppresses cell invasiveness, blocks VEGF production and induces thrombospondin, thereby inhibiting many of the signaling pathways and processes that contribute to angiogenesis and metastasis.

L5 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:515900 CAPLUS
DN 145:1037
TI Method and composition using agents increasing intracellular accumulation of NADH + H+ for enhancing anti-angiogenic therapy
IN Ben-Sasson, Shmuel A.
PA Yissum Research Development Company of the Hebrew University of Jerusalem, Israel
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2006056889 | A2 | 20060601 | WO 2005-IB4069 | 20051005 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,

SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRAI US 2004-616348P P 20041006
AB The invention relates to the discovery that agents that increase intracellular accumulation of NADH + H+ enhance the anticancer effects of angiogenesis inhibitors. Furthermore, treatment of a mammal with a combination of at least one angiogenesis inhibitor and at least one agent that enhances intracellular accumulation of NADH + H+ allows for the enhanced treatment and/or prevention of angiogenic diseases and disorders.

L5 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1005963 CAPLUS
DN 143:279399
TI antiangiogenic compounds for treating disorders associated with vascular permeability
IN Soker, Shay; Satchi-Fainaro, Ronit
PA USA
SO U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of Appl. No. PCT/US03/11265. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2005203013 | A1 | 20050915 | US 2004-962723 | 20041012 |
| WO 2003086178 | A2 | 20031023 | WO 2003-US11265 | 20030411 |
| WO 2003086178 | A3 | 20040108 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-371841P P 20020411
WO 2003-US11265 A2 20030411
AB The invention relates to methods for decreasing or inhibiting disorders associated with vascular hyperpermeability and to methods of screening for compds. that affect permeability, angiogenesis and stabilize tight junctions. In one aspect of the invention there is provided a method of decreasing or inhibiting vascular hyperpermeability in an individual in need of such treatment. The method includes administering to the individual an effective amount of an antiangiogenic compound selected from the group consisting of endostatin, thrombospondin, angiostatin, tumstatin, arrestin, recombinant EPO and polymer conjugated TNP-470. Other antiangiogenic compds. are disclosed herein.

L5 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:294991 CAPLUS
DN 143:19427
TI Inhibition of vessel permeability by TNP-470 and its polymer conjugate, caplostatin
AU Satchi-Fainaro, Ronit; Mamluk, Roni; Wang, Ling; Short, Sarah M.; Nagy,

Janice A.; Feng, Dian; Dvorak, Ann M.; Dvorak, Harold F.; Puder, Mark; Mukhopadhyay, Debabrata; Folkman, Judah

CS Vascular Biology Program, Department of Surgery, Children's Hospital Boston and Harvard Medical School, Karp Family Research Laboratories, Boston, MA, 02115, USA

SO Cancer Cell (2005), 7(3), 251-261
CODEN: CCAECI; ISSN: 1535-6108

PB Cell Press

DT Journal

LA English

AB Angiogenesis inhibitors, such as TNP-470 and the nontoxic HPMA copolymer-TNP-470 (caplostatin), are emerging as a class of anticancer drugs. The authors report that TNP-470 and caplostatin inhibit vascular hyperpermeability of tumor blood vessels as well as that induced in mouse skin by different mediators. Treatment with TNP-470 or angiostatin for 3 days was sufficient to reduce permeability of tumor blood vessels, delayed-type hypersensitivity, and pulmonary edema induced by IL-2. TNP-470 also inhibited VPF/VEGF-induced phosphorylation of VEGFR-2, calcium influx, and RhoA activation in endothelial cells. These results identify an activity of TNP-470, that of inhibiting vessel hyperpermeability. This activity likely contributes to TNP-470's antiangiogenic effect and suggests that caplostatin can be used in the treatment of cancer and inflammation.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:1036851 CAPLUS

DN 142:696

TI Synergistic treatment of cancer using immunomers in conjunction with chemotherapeutic agents

IN Kandimalla, Ekambar R.; Agrawal, Sudhir; Wang, Daqin

PA Hybridon, Inc., USA

SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

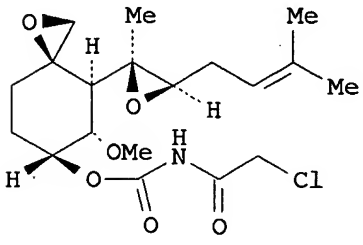
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004103301 | A2 | 20041202 | WO 2004-US15313 | 20040514 |
| | WO 2004103301 | A3 | 20051103 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2004241093 | A1 | 20041202 | AU 2004-241093 | 20040514 |
| | CA 2526212 | AA | 20041202 | CA 2004-2526212 | 20040514 |
| | US 2005009773 | A1 | 20050113 | US 2004-846167 | 20040514 |
| | EP 1628531 | A2 | 20060301 | EP 2004-752345 | 20040514 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |

PRAI US 2003-471247P P 20030516
WO 2004-US15313 W 20040514
OS MARPAT 142:696
AB The invention discloses the therapeutic use of immunostimulatory oligonucleotides and/or immunomers in combination with chemotherapeutic agents to provide a synergistic therapeutic effect.

L5 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:999688 CAPLUS
DN 141:428019
TI TNP-470 species polymer conjugates preparation as angiogenesis inhibitors
IN Satchi-Fainaro, Ronit; Folkman, Judah
PA Children's Medical Center Corporation, USA
SO U.S. Pat. Appl. Publ., 30 pp., Cont.-in-part of Appl. No. PCT/US03/10976.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2004229945 | A1 | 20041118 | US 2004-783986 | 20040219 |
| US 6949584 | B2 | 20050927 | | |
| WO 2003086382 | A1 | 20031023 | WO 2003-US10976 | 20030410 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2006020024 | A1 | 20060126 | US 2005-185538 | 20050720 |
| PRAI US 2002-371791P | P | 20020411 | | |
| US 2002-414705P | P | 20020930 | | |
| WO 2003-US10976 | A2 | 20030410 | | |
| US 2004-783986 | A1 | 20040219 | | |

OS MARPAT 141:428019
GI




I

AB The present invention relates to conjugates of water-soluble polymers and o-(chloracetyl-carbamoyl) fumagillol (TNP-470) (I) and use of those conjugates as specific intracellular carriers of the TNP-470 into tumor vessels. The present invention further relates to use of those conjugates to lower the neurotoxicity of TNP-470. Most preferably, the polymer has a mol. weight in the range of 15 kDa to 40 kDa. A random copolymer of HPMA and

methacryloyl-Gly-Phe-Leu-Gpy p-nitrophenyl ester was prepared, treated with ethylenediamine linker, and then with I to give the conjugate. Antitumor and angiogenesis activity of the conjugate were given.
RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:161479 CAPLUS
DN 140:368238
TI Targeting angiogenesis with a conjugate of HPMA copolymer and TNP-470
AU Satchi-Fainaro, Ronit; Puder, Mark; Davies, John W.; Tran, Hai T.; Sampson, David A.; Greene, Arin K.; Corfas, Gabriel; Folkman, Judah
CS Vascular Biology Program and Department of Surgery, Boston Children's Hospital and Harvard Medical School, Boston, MA, 02115, USA
SO Nature Medicine (New York, NY, United States) (2004), 10(3), 255-261
CODEN: NAMEFI; ISSN: 1078-8956
PB Nature Publishing Group
DT Journal
LA English
AB Angiogenesis is crucial for tumor growth. Angiogenesis inhibitors, such as O-(chloroacetyl-carbamoyl) fumagillol (TNP-470), are thus emerging as a new class of anticancer drugs. In clin. trials, TNP-470 slowed tumor growth in patients with metastatic cancer. However, at higher doses necessary for tumor regression, many patients experienced neurotoxicity. We therefore synthesized and characterized a water-soluble conjugate of N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer, Gly-Phe-Leu-Gly linker and TNP-470. This conjugate accumulated selectively in tumor vessels because of the enhanced permeability and retention (EPR) effect. HPMA copolymer-TNP-470 substantially enhanced and prolonged the activity of TNP-470 in vivo in tumor and hepatectomy models. Polymer conjugation prevented TNP-470 from crossing the blood-brain barrier (BBB) and decreased its accumulation in normal organs, thereby avoiding drug-related toxicities. Treatment with TNP-470 caused weight loss and neurotoxic effects in mice, whereas treatment with the conjugate did not. This new approach for targeting angiogenesis inhibitors specifically to the tumor vasculature may provide a new strategy for the rational design of cancer therapies.
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

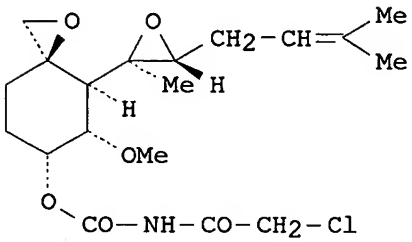
L5 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:836837 CAPLUS
DN 139:328369
TI TNP-470 conjugates with HPMA copolymer as angiogenesis inhibitors
IN Satchi-Fainaro, Ronit; Folkman, Judah
PA Children's Medical Center Corporation, USA
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003086382 | A1 | 20031023 | WO 2003-US10976 | 20030410 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

| | | | | | |
|---|---|---|---|---|---|
| | LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2480666 | AA | 20031023 | CA 2003-2480666 | 20030410 |
| | AU 2003230852 | A1 | 20031027 | AU 2003-230852 | 20030410 |
| | EP 1494662 | A1 | 20050112 | EP 2003-723958 | 20030410 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | US 2005169881 | A1 | 20050804 | US 2003-511009 | 20030410 |
| | JP 2005529870 | T2 | 20051006 | JP 2003-583402 | 20030410 |
| | US 2004229945 | A1 | 20041118 | US 2004-783986 | 20040219 |
| | US 6949584 | B2 | 20050927 | | |
| | US 2006020024 | A1 | 20060126 | US 2005-185538 | 20050720 |
| PRAI | US 2002-371791P | P | 20020411 | | |
| | US 2002-414705P | P | 20020930 | | |
| | WO 2003-US10976 | W | 20030410 | | |
| | US 2004-783986 | A1 | 20040219 | | |

GI




I

AB The present invention relates to conjugates of water-soluble polymers and o-(chloracetylcarbamoyl)fumagillol (TNP-470) and use of those conjugates as specific intracellular carriers of the TNP -470 into tumor vessels. The present invention further relates to use of those conjugates to lower the neurotoxicity of TNP-470. Most preferably, the polymer has a mol. weight in the range of 15 kDa to 40 kDa. HPMA copolymer with methacryloyl-Gly-Phe-Leu-Gly p-nitrophenyl ester was prepared, aminolyzed with ethylene diamine and reacted with TNP-470 (I) to give the conjugate . The conjugate was tested for antitumor activity and angiogenesis inhibition in the Miles assay.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:836749 CAPLUS
DN 139:302515
TI Methods for treating edema-related diseases by modulating vascular hyperpermeability, angiogenesis and tight junctions
IN Soker, Shay; Satchi-Fainaro, Ronit
PA Children's Medical Center Corporation, USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003086178 | A2 | 20031023 | WO 2003-US11265 | 20030411 |
| | WO 2003086178 | A3 | 20040108 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2480809 | AA | 20031023 | CA 2003-2480809 | 20030411 |
| | AU 2003226349 | A1 | 20031027 | AU 2003-226349 | 20030411 |
| | EP 1494699 | A2 | 20050112 | EP 2003-746738 | 20030411 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | JP 2006506321 | T2 | 20060223 | JP 2003-583209 | 20030411 |
| | US 2005112063 | A1 | 20050526 | US 2004-962901 | 20041012 |
| | US 2005203013 | A1 | 20050915 | US 2004-962723 | 20041012 |
| PRAI | US 2002-371841P | P | 20020411 | | |
| | WO 2003-US11265 | W | 20030411 | | |

AB The present invention relates to methods for decreasing or inhibiting disorders associated with vascular hyperpermeability and to methods of screening for compds. that affect permeability, angiogenesis and stabilize tight junctions. In one aspect of the present invention there is provided a method of decreasing or inhibiting vascular hyperpermeability in an individual in need of such treatment. The method includes administering to the individual an effective amount of an antiangiogenic compound selected from the group consisting of endostatin, thrombospondin, angiostatin, tumstatin, arrestin, recombinant EPO and polymer conjugated TNP-470. Other antiangiogenic compds. are disclosed herein.

L5 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:750448 CAPLUS
DN 139:281208
TI Targeting of myocardial angiogenesis through CD13/APN conjugates and use for diagnosis and therapy of cardiovascular diseases
IN Demuinck, Ebo D.; Shapiro, Linda H.
PA Cardiovascular Research Institute Maastricht, Neth.; St. Jude Children's Research Hospital
SO Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DT Patent
LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 1346729 | A1 | 20030924 | EP 2002-76146 | 20020319 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | WO 2003078569 | A2 | 20030925 | WO 2003-NL207 | 20030319 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, | | | | |

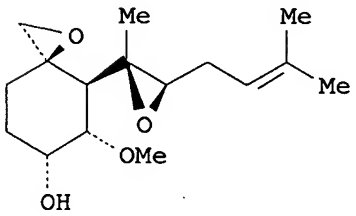
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| | AU 2003225405 | A1 | 20030929 | AU 2003-225405 | 20030319 |
| PRAI | EP 2002-76146 | A | 20020319 | | |
| | US 2002-365190P | P | 20020319 | | |
| | WO 2003-NL207 | W | 20030319 | | |

AB The present invention relates to conjugates comprising a CD13/APN homing mol. that is conjugated with a moiety for treating or diagnosing a cardiovascular disease. The invention further relates to methods in which these conjugates are used to target therapeutic agents or imaging mols. to the cardiovascular system. In particular the invention relates to conjugates comprising a CD13/APN homing mol. that is conjugated with angiogenesis-promoting factors for use in the treatment of ischemic myocardium or extremities. The invention also relates to conjugates comprising a CD13/APN homing mol. that is conjugated with a moiety that favorably alters wound healing after percutaneous arterial intervention. The invention further relates to conjugates comprising a CD13/APN homing mol. that is conjugated with a moiety that favorably alters atherosclerotic plaques, such as an angiogenesis inhibitor, for use in stabilizing or reducing the size of atherosclerotic plaques. Finally, the invention relates to conjugates comprising a CD13/APN homing mol. that is conjugated with an imaging moiety for use in diagnostic methods comprising vascular imaging.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:101908 CAPLUS
DN 138:401909
TI Concise stereocontrolled routes to fumagillol, fumagillin, and TNP -470
AU Vosburg, David A.; Weiler, Sven; Sorensen, Erik J.
CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Chirality (2003), 15(2), 156-166
CODEN: CHRLEP; ISSN: 0899-0042
PB Wiley-Liss, Inc.
DT Journal
LA English
OS CASREACT 138:401909
GI




I

AB A concise, diastereoselective synthesis of (±)-fumagillol (I) and formal, enantioselective syntheses of the potent angiogenesis inhibitors fumagillin and TNP-470 are reported. The origin of asymmetry is a highly diastereoselective Diels-Alder reaction using a

diene with a chiral oxazolidinone auxiliary. The stereochem. course of a key conjugate addition reaction is controlled by the cup-shaped architecture of a cis-fused bicyclic enal. Other key steps include a facile hetero-Claisen rearrangement and a site-selective Sharpless epoxidn.

RE.CNT 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:935435 CAPLUS
DN 136:84677
TI Methods for enhancing antibody-induced cell lysis and treating cancer
IN Weiner, George; Hartmann, Gunther
PA University of Iowa Research Foundation, USA
SO PCT Int. Appl., 312 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001097843 | A2 | 20011227 | WO 2001-US20154 | 20010622 |
| | WO 2001097843 | A3 | 20030123 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2410371 | AA | 20011227 | CA 2001-2410371 | 20010622 |
| | US 2003026801 | A1 | 20030206 | US 2001-888326 | 20010622 |
| | EP 1296714 | A2 | 20030402 | EP 2001-948684 | 20010622 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | JP 2003535907 | T2 | 20031202 | JP 2002-503327 | 20010622 |
| PRAI | US 2000-213346P | P | 20000622 | | |
| | WO 2001-US20154 | W | 20010622 | | |

AB The invention relates to methods and products for treating cancer. In particular the invention relates to combinations of nucleic acids and antibodies for the treatment and prevention of cancer. The invention also relates to diagnostic methods for screening cancer cells.

L5 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:824135 CAPLUS
DN 134:21434
TI Enzyme-activated antitumor prodrug compounds
IN Firestone, Raymond A.; Telan, Leila A.
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2000069472 | A2 | 20001123 | WO 2000-US10327 | 20000417 |
| | WO 2000069472 | A3 | 20010531 | | |
| | W: CA, JP, MX | | | | |

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

| | | | | | |
|---|---|---|---|---|---|
| | CA 2370245 | AA | 20001123 | CA 2000-2370245 | 20000417 |
| | EP 1181055 | A2 | 20020227 | EP 2000-923446 | 20000417 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | JP 2002544242 | T2 | 20021224 | JP 2000-617932 | 20000417 |
| PRAI | US 1999-134135P | P | 19990514 | | |
| | WO 2000-US10327 | W | 20000417 | | |

AB Disclosed are enzyme-activated antitumor and antimetastatic prodrug compds. The specific enzymes are collagenase(IV) and elastase. The conjugate N-Cbz-Gly-Phe-Ala-Leu-doxorubicin was prepared and the cleavage of this and other conjugates by enzymes was determined

L5 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:226788 CAPLUS
DN 120:226788
TI Drug delivery using biodegradable microspheres
AU Okada, Hiroaki; Yamamoto, Masaki; Heya, Toshiro; Inoue, Yayoi; Kamei, Shigeru; Ogawa, Yasuaki; Toguchi, Hajime
CS DDS Res. Lab., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SO Journal of Controlled Release (1994), 28(1-3), 121-9
CODEN: JCREEC; ISSN: 0168-3659
DT Journal
LA English
AB Rational delivery systems for leuprorelin acetate, a potent LHRH agonist, were achieved by developing a microsphere system using biodegradable polymers, poly(lactic/glycolic acid) (PLGA) and poly(lactic acid), which release the drug in a sustained-release fashion depending on the biodegrdn. of polymer used and persistently suppress steroidogenesis for over 1 and 3 mo, resp., following a single injection. To produce these systems, the authors established a novel microencapsulation technique, the in-water drying method, and microspheres with a high trap ratio and small initial burst were obtained. A microsphere system of TRH prepared using PLGA could also continuously release the drug for 2 or 4 wk. Using these systems effectively reduced the required dose compared with that needed with daily injection due to more continuous receptor hits on the target organs and could improve patient compliance. Chemoembolization using PLGA microspheres containing an angiogenesis inhibitor, TNP-470, resulted in dramatic regression of VX-2 carcinoma in rabbits. The microsphere system using biodegradable polymers is useful in designing controlled release delivery and targeted delivery to attain potent and rational therapy.

=> log y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 57.25 | 57.46 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -12.75 | -12.75 |

STN INTERNATIONAL LOGOFF AT 14:57:08 ON 02 OCT 2006